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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/869,630
Filing Date: September 21, 2001
Appellant(s): KNOX ET AL.

Craig Bohlken
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 17, 2007 appealing from the Office action mailed July 25, 2007.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,015,565	Rose et al.	1-2000
6,426,058	Pines et al.	7-2002

For the above reasons, it is believed that the rejections should be sustained.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 1 and 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rose et al., 6,015,565, in view of Pines et al., 6,426,058.

Rose et al. disclose the invention substantially as claimed.

More specifically, as to claims 1 and 10, Rose et al. disclose an in vitro method which is a test involving a reaction of one or more biological molecules (col. 49, lines 19-21) and which comprises:

conducting said reaction (col. 49, lines 1-25); and

observing a magnetic response resonance spectrum and/or NMR image of the label during the course of said reaction in order to detect a conformational change in the labeled biological molecule (col. 49, lines 32-35),wherein one of said one or more biological molecules comprises an assay reagent (i.e., the pharmaceutical candidate or alternatively the Glycoprotein B, see col. 49, lines 19-21);

Although Rose et al. teach use of NMR in general to detect a conformational change due to the binding of the candidate to the Glycoprotein B, Rose et al. however does not explicitly disclose labeling the biological moleuce with hyperpolarized ^{129}Xe to enhance NMR detection. Pines et al. however disclose this limitation.

Pines et al. teach use of NMR spectroscopy for determining structure and conformation of molecules (col. 1, lines 18-22) to analyze, characterize or image a

biological sample (col. 12, lines 6-13; and col. 18, lines 61-64.) Pines et al. teach a method of measuring a signal transferred from a hyperpolarized noble gas atom to a no-noble gas NMR active nucleus such as ^{13}C or ^{15}N (col. 15, lines 26-39). Pines et al. teach that the detection is used to study regions of a structure that bind to or otherwise interact with the hyperpolarized noble gas. Such detection is used to study a macromolecule such as a protein (col. 15, line 62 – col. 16, line 6). Pines et al. teach further teaches that hyperpolarization of an NMR active nucleus enhances the noble gas magnetic resonance signal (column 1, lines 12-14; col. 18, lines 31-32.) Furthermore Pines et al. teach that a preferred hyperpolarized noble gas is ^{129}Xe (col. 7, lines 53-54 and col. 9, lines 6-10.) Pines et al. teaches that hyperpolarized xenon can be used to elucidate structures of biologically relevant molecules, such as proteins, by selective polarization transfer to the protons of the specific sites where the xenon binds (col. 30, lines 38-41.)

It would have been obvious to one of ordinary skill in the art to utilize hyperpolarized ^{129}Xe as taught by Pines et al. in the Rose et al. NMR detection of a binding or conformation change because Pines et al. teach that using hyperpolarized ^{129}Xe will enhance the magnetic resonance signal, as would be desirable for obtaining more accurate results.

As to the following claims, Rose et al. teach the limitations as follows.

As to claims 3 and 4, the assay is a binding assay (col. 49, lines 32-35.)

As to claim 5, the molecule is a protein (col. 49, lines 32-33.)

And as to claims 6-9, Rose et al. also does not disclose that the hyperpolarized ^{129}Xe is enriched at a level of 40% or more, or that the degree of hyperpolarisation is 8% or more, or that the method is performed in a solution wherein the solvent has a viscosity in the range of 700 to 1500 mPs, or that the pressure of the xenon gas is at least 5 bar.

Since these claimed ranges are optimum or workable ranges, it would have been obvious to modify the Rose et al. reference to provide these ranges because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum of workable ranges involves only routine skill in the art (In re Aller, 105 USPQ 233.)

(10) Response to Argument

Appellants argue on pages 4-5 that Rose does not teach, disclose or suggest that the nuclear magnetic resonance (NMR) spectrum and/or image is observed during the course of the reaction between the candidate and glycoprotein B. Appellants assert that the detection step of Rose is temporally separate to the reaction itself.

Examiner points out that Rose teaches that binding of the candidate to the Glycoprotein B may be observed as a conformational change, detected for example by nuclear magnetic resonance (see column 49, lines 32-35). Observation of a conformational change involves observation of at least the compound before contact with the candidate, and observation of the compound after contact. While Rose refers to

nuclear magnetic resonance as a detection technique in general and does not go into details about the detection technique, the skilled artisan would understand that nuclear magnetic resonance involves observation of a spectrum and thus to observe a change involves observing a change in the spectrum. This is supported by the disclosure of Pines. Pines teaches nuclear magnetic resonance spectroscopy for analyzing a sample (col. 3, lines 35-51), and that hyperpolarized gases are useful both as tracers, which are themselves detected, and also as agents which affect the magnetic properties of other nuclei present in a sample (col. 3, lines 37-40). Pines also teaches that hyperpolarization of the noble gases (such as ^{129}Xe) enhances the sensitivity of NMR which allows for better determination of the primary structure, conformation and local dynamic properties of the molecules in a liquid solution (col. 7, lines 53 – col. 8, line 8.) While the examples given by Pines do not involve a reaction, such as that disclosed by Rose, the examples given by Pines disclose that nuclear magnetic resonance detection technique involves observing a spectrum. For example in column 5, lines 21-23, Pines discloses the time dependence of the hyperpolarized ^{129}Xe NMR signal observed in benzene solution after being contacted with hyperpolarized xenon, thus, disclosing that the NMR signal is time dependent. In column 21, lines 42-45, Pines discloses that the significantly improved signal-to-noise ratio obtained in spectra measured on samples containing polarized ^{129}Xe NMR spectra allows the real time observation of the dynamics of the transfer of the xenon from the saline/plasma mixture into the red blood cells.

Thus, Pines teaches that the NMR signal is time-dependent and results in a spectrum that allows for real time observation. In the NMR detection in the Rose method, there is no reason to believe that the skilled artisan would not detect the NMR spectrum for a period of time from before Glycoprotein B is contacted with the candidate, i.e., before a reaction, to *during* the contact step, i.e., during the reaction, including the end of the reaction. The skilled artisan would detect the NMR signals during this period of time since the skilled artisan is looking to observe the change in the spectrum, which is time-dependent, to determine a conformational change upon binding.

Appellants also state on pages 6-7 of the appeal brief that it is difficult to believe that Rose would even suggest improving its invention by labeling a biological molecule with hyperpolarized ^{129}Xe to enhance NMR detection, and that Examiner's reasoning ignores the fact that Rose gives no description at all about labeling a biological molecule with hyperpolarized ^{129}Xe to enhance NMR detection but expounds at length about the other features of the invention. Appellants contend that Examiner has failed to show why the person skilled in the art would select only labeling a biological molecule with hyperpolarized ^{129}Xe to enhance NMR detection from the long list of features in the Rose invention, as listed on page 6 of the appeal brief, and as a consequence choose not to improve all the other aspects even those which Rose teaches as important.

Appellants' arguments appear to imply that improving the NMR detection technique would necessarily exclude any improvements in any other aspects of the invention, or that the ground for rejection asserts that the skilled artisan would make no

improvements to the Rose invention other than the improvement of the NMR detection step. As to the latter, the grounds for rejection does not state or imply that other improvements to the Rose invention are excluded. As to the former, there is no reason to believe that the skilled artisan cannot improve other aspects of the Rose invention in addition to improving the detection step. In any case, there is no reason why the skilled artisan would not choose to improve just the detection step.

Appellants' arguments also appear to imply that the detection step is not important in the Rose invention since the Rose invention involves a long list of features, as summarized by Appellants on page 6 of the brief, the list including isolating polynucleotides...obtaining polynucleotides comprising linear sequences of amino acids; isolating..... Examiner contends however the detection step is the whole point of the Rose invention and thus is actually a very important step. The Rose reaction in column 49, lines 1-25, to which the Office action refers, discloses that the method involves combining an active Glycoprotein B with the pharmaceutical candidate, and determining whether the biochemical function is altered by the pharmaceutical candidate. Column 49, lines 32-35, in the Rose reference further discloses that one embodiment of the screening method is to measure binding of the pharmaceutical candidate directly to the isolated Glycoprotein B. Compounds that bind to an active site of the molecule are expected to interfere with Glycoprotein B activity. Rose disclose that binding of the candidate to the Glycoprotein B may be observed as a conformational change, detected for example by nuclear magnetic resonance (column 49, lines 32-35). Thus, contrary to Appellants' argument, the detection step, which

determines whether the pharmaceutical candidate binds to the Glycoprotein B and thus interferes with Glycoprotein B activity, is an important step since this is ultimately what is of interest.

Appellants also argue on page 8 that by teaching positively towards certain embodiments or features as being important or preferred, the art provides a motivation for the person skilled in the art to go in a particular direction, and if that direction leads towards subject matter outside the scope of the claims at issue, then it constitutes a "teaching away". Appellants maintain that the person skilled in the art would focus on the specific teachings in Rose of embodiments taught to be important, and be motivated to improve those elements. Appellants state that Rose teaches combining a pharmaceutical candidate with glycoprotein B and thereafter detecting whether the pharmaceutical candidate has bound to the active site of glycoprotein B to be important. Appellants emphasize that Rose devotes about 59 columns of text to what is the essence of his invention, the use of combining a pharmaceutical candidate with glycoprotein B, and does not teach, suggest, or disclose using NMR spectrum and/or any image observable during the course of the reaction between the candidate and glycoprotein B. This is not persuasive because as indicated above the detection step is what is of interest and thus is a very important step. The skilled artisan would be motivated to improve the detection step as this would provide for more accurate results. Rose discloses using nuclear magnetic resonance (NMR) for the detection, and Pines teaches an improvement to NMR detection technique, and that such improvements enhance the sensitivity of NMR and therefore allow for better determination of the

primary structure, conformation and local dynamic properties of the molecules in a liquid solution (col. 8, lines 5-9), and significantly improves the signal-to-noise ratio (column 21, lines 42-45). Thus the skilled artisan would be motivated to improve the detection step in the Rose invention as it would provide for more accurate results by enhancing the sensitivity of the NMR detection, i.e., the detection of the binding of which is the whole purpose of the Rose method. Thus, Appellants' arguments are not persuasive.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

Ann Lam

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